Meeting Report: Hereditary Breast and Ovarian Cancer (HBOC): Risks and Challenges

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Some hereditary breast and ovarian cancers have been shown to be related to inherited gene mutations in BRCA1 or BRCA2 genes. These two genes are key tumor suppressors with a role in cellular DNA repair, genomic stability, and checkpoint control. Current understanding of the pathogenesis, epidemiology, genetic factors and clinical interventions from this group of patients has resulted in significant impact on our more general understanding of breast and ovarian cancers. Recent methodologies revealing molecular subtypes among these cancers have engendered interest in treatment and prevention of these syndromes, however, despite advances in diagnostic and prognostic approaches, many questions remain.

In September 2009, the National Cancer Institute (NCI) of Bari and the NYU Cancer Institute organized the First Joint Meeting 'Hereditary Breast and Ovarian Cancers: Risks and Challenges' in collaboration with the American Italian Cancer Society, the Lynne Cohen Foundation for Ovarian Cancer Research, and the Lega Italiana per la Lotta contro i Tumori. Additionally the meeting was supported through an NIH grant (#1R13CA142030-01) and by the Alleanza Contro il Cancro. The meeting included 21 presentations, 8 selected abstract presentations and 3 selected poster discussions.

Three major themes were covered:

1. Susceptibility factors in breast cancer: BRCA1 and BRCA2 genes, unclassified variants and other genes that increase the breast cancer risk.
2. Clinical management of breast cancer patients and diagnostic methods for risk analysis.
3. Social and psychological aspects.

The impact of BRCA mutations on phenotypic expression in breast and ovarian cancer was reviewed. Previously published data has demonstrated the high frequency of BRCA1/2 un-

classified variants and polymorphisms in patients at high risk undergoing genetic testing. Paolo Radice (NCI Milan) reported an interesting approach to classification of the BRCA1 and 2 variants of uncertain significance that could lead to better understanding of function. Antonis Antoniou (Cambridge, UK) described the effort by the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA) to identify modifiers of risk, and showed the distribution of BRCA cumulative breast cancer risk by combined genotypes. About a possible role of BRCA1/2 polymorphisms, Brunella Pilato (NCI Bari) discussed a new study design analyzing the transmission of polymorphic haplotypes in family members of individual patients tested by genetic counselors. Innovative technologies for cancer risk analysis with novel rapid methods for BRCA1 and BRCA2 mutation identification, were presented by Stefania Tommasi (NCI Bari). In addition, PALB2 mutations have been shown to have a possible role in the pathogenesis of non-BRCA mutated hereditary cancers that lack BRCA mutations.

Angelo Paradiso (NCI, Bari) discussed the biological and clinical features of hereditary breast cancer. He reviewed the increased level of risk conferred by pre-neoplastic lesions, and the need to optimize the therapeutic approach through a better definition of clinical outcome. Two issues were presented regarding mammographic density and magnetic resonance imaging (MRI). MRI showed a positive predictive value in BRCA mutated patients and Franca Podo (Rome) reported the results of a multicentric study performed from 2000 to 2008 at major Italian centers. The Italian group study was consistent with the Toronto experience, where only one interval cancer developed in studies published by Warner et al. Dr. Warner reported these findings, and from her group there was also a presentation of why a large number of these women opt for bilateral mastectomies rather than continued follow up.

There were enticing presentations about emerging pharmacological opportunities in cancer prevention, Hilary Calvert (University College, London) updated the possible development of PARP inhibitors as potentially useful therapeutic agents against BRCA mutated tumors. Julia Smith (NYU) presented a study on a novel somatostatin analog (SOM230) that has demonstrated reversal of preneoplastic lesions in women at high risk for development of breast cancer. Nutritional concerns in possibly modifying underlying genetic risks

were discussed by Niva Shapira (Ramat Aviv, Israel). Social and psychological aspects related to risk in breast and ovarian cancer patients were discussed, and Antonella Surbone (NYU) raised ethical, legal and social issues of the 'asymptomatic ill'.

The 2nd Joint Meeting of the organization is scheduled for March 2011 and will provide a forum for further exploration of current and future clinical and laboratory studies.